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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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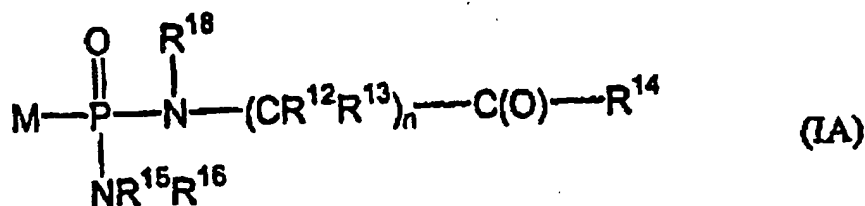
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(54) Title: NOVEL BISAMIDATE PHOSPHONATE PRODRUGS



(57) Abstract: Novel bisamidate phosphonate prodrugs of FBPase inhibitors of the Formula (IA) and their use in the treatment of diabetes and other conditions associated with elevated blood glucose.

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07F9/655 A61K31/66 A61P3/10 C07F9/44 C07F9/6561
C07F9/6558

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07F A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EP0-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 39342 A (METABASIS THERAPEUTICS) 11 September 1998 (1998-09-11) cited in the application the whole document ---	1-115
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Y	WO 98 39344 A (METABASIS THERAPEUTICS) 11 September 1998 (1998-09-11) cited in the application the whole document ---	1-115
Y	WO 95 07920 A (GILEAD SCIENCES) 23 March 1995 (1995-03-23) the whole document ---	1-115
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 45016 A (METABASIS THERAPEUTICS) 10 September 1999 (1999-09-10) the whole document ----	1-115
P,Y	WO 00 14095 A (METABASIS THERAPEUTICS) 16 March 2000 (2000-03-16) cited in the application the whole document ----	1-115
P,X	WO 00 38666 A (METABASIS THERAPEUTICS) 6 July 2000 (2000-07-06) the whole document -----	1-115

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1-3 refer to compounds of formula IA in which a substituent M is present.

As no definition is given for such substituent in any of claims 1-3, the search has been performed according to the definitions of M given in claims 4-57, 62-100, 103-110 and in the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9839342 A	11-09-1998	AU 6691798 A US 6054587 A	22-09-1998 25-04-2000
WO 9839343 A	11-09-1998	AU 6691498 A EP 0970095 A US 6110903 A	22-09-1998 12-01-2000 29-08-2000
WO 9839344 A	11-09-1998	AU 6452098 A	22-09-1998
WO 9507920 A	23-03-1995	US 5656745 A AU 691527 B AU 7875294 A AU 690587 B AU 7956594 A BR 9407510 A EP 0719273 A EP 0719274 A JP 9506333 T JP 9506334 T WO 9507919 A US 6225460 B US 5886179 A US 5591851 A US 5798340 A US 5756486 A	12-08-1997 21-05-1998 03-04-1995 30-04-1998 03-04-1995 07-01-1997 03-07-1996 03-07-1996 24-06-1997 24-06-1997 23-03-1995 01-05-2001 23-03-1999 07-01-1997 25-08-1998 26-05-1998
WO 9945016 A	10-09-1999	AU 3069999 A EP 1060182 A	20-09-1999 20-12-2000
WO 0014095 A	16-03-2000	AU 1090500 A EP 1112275 A NO 20011174 A	27-03-2000 04-07-2001 09-05-2001
WO 0038666 A	06-07-2000	AU 2058300 A	31-07-2000